

AD\_\_\_\_\_

Award Number: DAMD17-03-2-0028

TITLE: A Randomized Placebo-Controlled Trial of Citalopram for Anxiety Disorders Following Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Michael Jaffee

CONTRACTING ORGANIZATION: Henry M Jackson Foundation for the  
Advancement of Military Medicine  
Rockville MD 20852

REPORT DATE: April 2008

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. <b>PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.</b>					
1. REPORT DATE (DD-MM-YYYY) 01-04-2008		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 01 Apr 07 – 31 Mar 08	
4. TITLE AND SUBTITLE A Randomized Placebo-Controlled Trial of Citalopram for Anxiety Disorders Following Traumatic Brain Injury				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER DAMD17-03-2-0028	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Michael Jaffee  E-Mail:				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)  Henry M Jackson Foundation for the Advancement of Military Medicine Rockville MD 20852				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT: The overarching goal of this project is to study the effects of a serotonin reuptake inhibitor (SRI), citalopram, for the treatment of anxiety experienced by individuals after traumatic brain injury (TBI). Specifically, this project seeks to treat individuals who meet criteria for DSM-IV diagnosis of Anxiety Disorder Due to a General Medical Condition, within 3 to 24 months of TBI. A randomized placebo controlled design with 1-year follow-up will be utilized to evaluate the effectiveness of citalopram in alleviating significant anxiety symptoms that cause significant distress and can lead to medical retirement of active duty soldiers.					
15. SUBJECT TERMS Traumatic Brain Injury; Anxiety Disorders; SRI Treatment; Randomized Controlled Trial					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	5	19b. TELEPHONE NUMBER (include area code)

## Table of Contents

<b>Introduction.....</b>	<b>4</b>
<b>BODY.....</b>	<b>4</b>
<b>Key Research Accomplishments.....</b>	<b>5</b>
<b>Reportable Outcomes.....</b>	<b>5</b>
<b>Conclusions.....</b>	<b>5</b>
<b>References.....</b>	<b>5</b>

**Introduction:**

The overarching goal of this project is to determine the effectiveness of citalopram for the treatment of anxiety disorders following Traumatic Brain Injury (TBI) and to examine possible longer term effectiveness of treatment with citalopram on symptom reporting and return to work/duty.

**Body:**

Participants who experienced a TBI 3 to 24 months ago and are experiencing anxiety are eligible for the study. If they agree to participate, they sign informed consent prior to research testing. An informational script about the study is read to individuals. After the script is read, the individual is given the informed consent to review. Patients are ineligible to participate in the study until they reach a Rancho Los Amigos level of 7 or 8. If there is any question as to a patient's capacity to consent, the neuropsychologist and/or psychiatrist involved in the study assesses the subject's level of comprehension prior to consent. Any confusional state prohibits a subject from being rated as a 7 or 8. After signing the informed consent, tests and scales are administered and patients are randomized to receive a 12-week course of citalopram or placebo. Female participants of childbearing potential are given a serum pregnancy test prior to randomization. If the test is positive, she is ineligible for participation in the study.

Eligible, consented participants receive an increasing dose of citalopram, up to 40 mg, or placebo, up to 4 pills. A blood sample drawn after completion of the 12-week treatment period is used to obtain citalopram levels as a measure of medication compliance. A two-week taper follows the treatment period. Study participants receive comprehensive multidisciplinary evaluations at a DVBIC site, including neuropsychological and psychiatric interviews and evaluations at baseline, 12 weeks and 12 months.

Since the last annual report, there have been no modifications to the protocol.

There have been no new enrollments since the last report. The total number of subjects enrolled (or specimens used) over the entire study length is 19.

All subjects enrolled were male and had an active duty status. They were primarily Caucasian (84.2%), in the United States Army (57.9%), and single (52.6%). At the time of baseline evaluation, the mean age of subjects was 26.9 years (range 20-41 years). The mean number of years of education in the sample was 12.9 years (range 11-18 years).

The primary outcome measures for this study were the DSM-IV diagnostic criteria for Anxiety Disorder Due to General Medical Condition – both “caseness” and number of GAD symptoms, and the total score on the Spielberger State Anxiety Inventory.

Meeting the criteria for having an anxiety disorder was determined through an algorithm using the Hamilton Anxiety Scale (reference for this scale?). Of the 19 subjects evaluated at baseline, 17 met the DSM IV criteria of Anxiety Disorder Due to a General Medical Condition using the Hamilton Anxiety Scale algorithm. The remaining two subjects met criteria through the use of

the Structured Clinical Interview for DSM Disorders (SCID). Determination for diagnosis was completed by the Principal Investigator, psychiatrist, physician assistant, or nurse. Of the 15 subjects evaluated at the Week 12 evaluation, 11 met the criteria for an anxiety disorder using the Hamilton Anxiety Scale algorithm. Of the remaining four, two met criteria through the use of the SCID, and two did not meet criteria for the disorder.

The Spielberger State Anxiety Inventory consists of 20 items that ask how a person feels now, and reflects situational factors that may influence anxiety levels. Scores range from 20 to 80 and the higher the score the greater the level of anxiety. For subjects who completed both a Baseline and Week 12 evaluation, the mean total score at Baseline on the Spielberger State Anxiety Inventory was 42.7. The mean total score for the same group at the Week 12 evaluation was 42.3.

### **Key Research Accomplishments:**

Data has been completely entered or is in the process of being entered (for follow-up visits) into an electronic data capture system for 19 patients. Data continues to be monitored and quality controlled.

### **Reportable Outcomes:**

There have been no presentations or manuscripts completed in the past year in relation to this study.

### **Conclusion:**

Despite challenges in patient accrual in the past, we had been optimistic that we could enroll the remaining subjects during the past year with the expansion of the time-since-injury range. It became clear, however, that even with the change in inclusion criteria, the number of patients eligible at the time of screening was negligible. The investigators have learned that this study was not feasible during wartime due to medical providers prescribing selective serotonin reuptake inhibitors for soldiers immediately after their return from theater.

### **Recommendations:**

- [1] Complete the statistical analysis of all the accrued patients – timeframe for completion of this aspect of the study is expected to be end of May 2008
- [2] The program will remain open for any further data analysis at a no further cost
- [3] **The study will be closed to accrual as soon as the initial unblinded analysis is completed and the PI is signatory to the close out letter.**

### **References:**

Not Applicable